

## REMARKS/ARGUMENTS

### **1. Status of the Claims and Outstanding Objections/Rejections**

Claims 1-50 are pending in the above-referenced patent application; claims 1-50 are currently under examination. In the Office Action, the priority claim, the drawing descriptions for FIGS. 15 and 16 and the Abstract have been objected to for the reasons set forth hereinbelow. In addition, claims 1-10, 14-28 and 32-49 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 13, 31 and 50 have also been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 36-50 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. Finally, claims 18 and 35 have been rejected under the judicially created doctrine of obviousness-type double patenting. For the reasons set forth herein, each of the Examiner's objections/rejections is overcome.

### **2. Amendments**

Claims 1, 5, 13, 15, 19, 23, 31, 33, 36, 43 and 50 have been amended. More particularly, in accordance with the Examiner's suggestion, independent claims 1, 19 and 36 have been amended to delete "general" from the phrase "an aspartyl protease inhibitor having the general formula. . . ." Claims 15 and 33 have been amended to correct the minor errors in the claim dependencies noted by the Examiner. Dependent claims 5, 23 and 43 have been amended to correct a minor error in the structural formulae. Claims 13, 31 and 50 have been amended in accordance with the Examiner's suggestion to incorporate the chemical structures of the compounds CEL5-A, CEL5-G and EA-1. Independent claim 36 has been amended to incorporate the limitations of dependent claims 37 and 38. In view of the amendment to claim 36, Applicants have canceled, without prejudice to further prosecution, dependent claims 37 and 38. Such amendments relate to formal matters and, thus, no new matter has been introduced.

3. **The Priority Claim**

In the Office Action, the Examiner indicated that “[i]f applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application” (*see*, page 2 of the Office Action).

In order to expedite prosecution, Applicants have amended the first page of the specification to recite the priority information for the above-referenced patent application. It is noted that this priority information was set forth on the Application Data Sheet (ADS), under the heading “Domestic Priority Information,” which was filed, together with the above-referenced patent application, in the U.S.P.T.O. on February 5, 2004.

In view of the amendment to the specification, Applicants urge the Examiner to withdraw this objection.

4. **The Drawings**

In the Office Action, the Examiner indicated that “[t]he application contains drawings labeled Fig. 15A, 15B, 16A and 16B,” but “Applicants refer to Figures 15 and 16 only” (*see*, page 4 of the Office Action).

In order to expedite prosecution, Applicants have amended the descriptions of Figures 15 and 16 on page 10 of the specification to specifically refer to Figures 15A and 15B and Figures 16A and 16B, respectively. In view of the amendments to the descriptions of Figures 15 and 16, the Examiner’s concern is rendered moot. Accordingly, Applicants urge the Examiner to withdraw this objection.

5. **The Abstract**

In the Office Action, the abstract was objected to as allegedly being too short and generic (*see*, page 4 of the Office Action). The Examiner indicated that this objection could be overcome by amending the abstract to include, for example, claim 1.

In order to expedite prosecution, the abstract has been amended to include the subject matter recited in claim 1. In view of the amendment to the abstract, the Examiner’s concern is overcome. Accordingly, Applicants urge the Examiner to withdraw this objection.

**6. Objection to Claims 15 and 33**

In the Office Action, claims 15 and 33 were objected to under 37 C.F.R. § 1.75(c) as being in improper form for a multiply dependent claim.

In order to expedite prosecution of the present case, Applicants have amended claims 15 and 33 to delete reference to claims 13 and 31, respectively. As amended, claims 15 and 33 are in proper dependent form. Accordingly, Applicants urge the Examiner to withdraw this objection.

**7. Rejection Under 35 U.S.C. § 112, Second Paragraph**

a. Claims 1-10, 14-28 and 32-49 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite due to the use of the phrase “general formula” (*see*, page 5 of the Office Action). The Examiner indicated that this rejection can be overcome by amending claims 1, 19 and 36 to delete the word “general” (*see*, page 5 of the Office Action).

In order to expedite prosecution of the present case, Applicants have amended claims 1, 19 and 36 to delete the word “general.” In view of the amendments to claims 1, 19 and 33, the Examiner’s concern is overcome. Accordingly, Applicants urge the Examiner to withdraw this rejection.

b. Claims 1-10, 14-28 and 32-49 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite due to the use of the technical terms “substituted alkyl,” “substituted aryl” and “substituted heteroaryl” (*see*, page 5 of the Office Action). According to the Office Action, the definition of these terms in the specification allegedly “do not allow the public to understand the metes and bounds of the claims.” Applicants respectfully traverse the rejection.

The terms “substituted alkyl,” “substituted aryl” and “substituted heteroaryl” are clearly defined in the specification on page 11, lines 9-15 and lines 25-32, and page 13, lines 13-22. In addition, several examples of substituted alkyls, substituted aryls, and substituted heteroaryls are set forth in the specification (*see*, page 11, lines 9-15 and lines 25-32, and page 13, lines 13-22 of the specification). Clearly, one of skill in the art can identify other substituted

alkyls, substituted aryls, and substituted heteroaryls suitable for use in the present invention *without* undue experimentation. The claimed compound containing these substituted alkyls, substituted aryls, and substituted heteroaryls are aspartyl protease inhibitors of Formula I. The specification teaches one of skill in the art a number of procedures for testing the activity of such aspartyl protease inhibitors (*see*, page 31-36 of the specification). These assays include, for example, *in vitro* assays that assess the effects of test compounds on processing of APP, *in vivo* assays to evaluate the ability of compounds to modulate processing of APP, and assays to measure the ability of aspartyl protease inhibitors to modulate the processing of  $\tau$ -protein.

Since 1) the terms “substituted alkyl,” “substituted aryl” and “substituted heteroaryl” are terms of art that are routinely used by those of skill in the art; 2) such terms are defined in the specification as originally filed; 3) the claims are directed towards compounds that are aspartyl protease inhibitors of Formula I; and 4) the specification teaches a number of assays to test the activity of such compounds, the present invention clearly allows the public to understand the metes and bounds of the claims. In addition, Applicants would like to point out that a quick search of the term “substituted alkyl” in the claims of issued patents on the U.S.P.T.O. reveals that well over 11,500 U.S. Patents have issued with claims containing the term “substituted alkyl.” Similar numbers can be found for issued patents containing the terms “substituted aryl” and “substituted heteroaryl,” all of which point to the fact that such terms are terms of art that are routinely used by those of skill in the art. Therefore, Applicants respectfully request that the rejection be withdrawn.

c. Claims 13, 31 and 50 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for containing the phrase “CELS-A, CELS-G and EA-1, which are illustrated in FIG. 12” (*see*, page 6 of the Office Action). The Examiner indicated that this rejection can be overcome by amending the claims to recite the chemical structures of these three compounds (*see*, page 6 of the Office Action).

In order to expedite prosecution of the present case, Applicants have amended claims 13, 31 and 50 to recite the chemical structures of the compounds CEL5-A, CEL5-G and EA-1. In view of the amendments to claims 13, 31 and 50, the Examiner’s concern is overcome.

Accordingly, Applicants urge the Examiner to withdraw the rejection under 35 U.S.C. § 112, second paragraph.

8. **Rejection Under 35 U.S.C. § 112, First Paragraph**

Claims 36-50 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. In making this rejection, the Examiner has alleged that the scope of the phrase “neurodegenerative disorder” cannot be deemed enabled (*see*, page 7 of the Office Action).

In order to expedite prosecution of the present case, Applicants have amended independent claim 36 to recite the limitations of dependent claims 37 and 38. As amended, claim 36 is directed to a method for treating a neurodegenerative disorder the method comprising: administering to a mammal a therapeutically effective amount of an aspartyl protease inhibitor of Formula I, ***wherein said neurodegenerative disorder is characterized by the accumulation of amyloid plaques or by the accumulation of  $\tau$ -fragments.*** As stated in the specification, neurodegenerative disorders that can be treated using the aspartyl protease inhibitors of the present invention include, for example, those neurodegenerative disorders characterized by the accumulation of amyloid plaques or  $\tau$ -protein. It is well-known in the art that such plaques containing large amounts of A $\beta$ . Clearly, therapeutic agents that can decrease the formation of A $\beta$ , as do the aspartyl protease inhibitors of the present invention, can play a beneficial role in retarding the progression of these neurodegenerative disorders, ***wherein the neurodegenerative disorders are characterized by the accumulation of amyloid plaques or by the accumulation of  $\tau$ -fragments.*** Examples of such neurodegenerative diseases include, but are not limited to, the following: Alzheimer's disease, Parkinson's disease, cognition deficits, Downs Syndrome, cerebral hemorrhage with amyloidosis, dementia (*e.g.*, dementia pugilistica) and head trauma.

As explained above and as demonstrated in the specification, the aspartyl protease inhibitors of Formula I of the present invention can be used to modulate the processing of an APP and a  $\tau$ -protein. Thus, claims 36 and 39-50 are directed to a method of treating neurodegenerative disorders, ***wherein the neurodegenerative disorders are characterized by the***

*accumulation of amyloid plaques or by the accumulation of  $\tau$ -fragments*, and the specification clearly provides evidence that points to an activity for the aspartyl protease inhibitors of Formula I that is consistent with the claimed method of use. As such, the rejection under 35 U.S.C. § 112, first paragraph, is improper and should be withdrawn.

**9. Obviousness-type Double Patenting Rejection**

Claims 18 and 35 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 13-34 of U.S. Patent No. 6,150,416. The Examiner indicated that this rejection can be overcome by filing a Terminal Disclaimer (*see*, pages 12 and 13 of the Office Action).

Applicants respectfully request that this obviousness-type double patenting rejection be held in abeyance until Applicants receive from the Examiner an indication regarding allowable subject matter. At that time, Applicants will file a Terminal Disclaimer as suggested by the Examiner or, alternatively, cancel the conflicting claims.

**10. Allowable Subject Matter**

Applicants acknowledge, with appreciation, the Examiner's indication (1) that claims 11, 12, 29 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims; and (2) that claims 1-10, 13-17, 19-28 and 31-34 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. § 112, second paragraph, set forth in the Office Action (*see*, page 13 of the Office Action). In view of the above remarks and amendments to the claims, Applicants believe the outstanding objections/rejections have been overcome, thereby placing all of the pending claims in condition for allowance.

Appl. No. 10/774,262  
Amdt. dated June 2, 2005  
Reply to Office Action of December 2, 2004

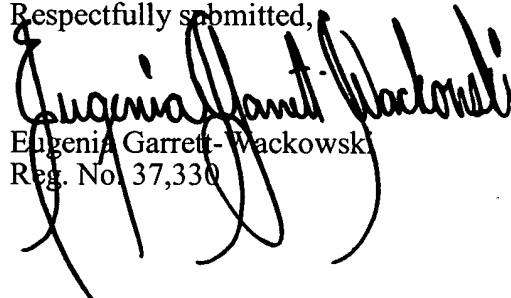
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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Eugenia Garrett-Mackowski", is written over the typed name and registration number.

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